

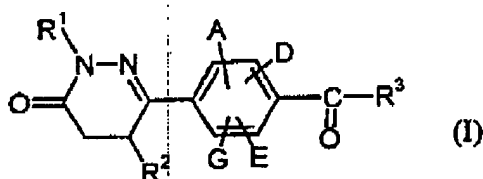
Application No. 10/018,827
Amdt. dated 17 March 2003

Attorney Docket No. LeA 33783

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims: ✓

1. (currently amended) A 6-carboxyphenyldihydropyridazinone derivative of the general formula (I)



in which

A, D, E and G are identical or different and represent hydrogen, halogen, trifluoromethyl or hydroxyl, or represent (C₁-C₆)-alkyl or represent (C₁-C₆)-alkoxy,

R¹ and R² are identical or different and represent hydrogen or represent (C₁-C₆)-alkyl,

R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

in which

R⁴ denotes cycloalkyl having from 3 to 8 carbon atoms or (C₁-C₈)-alkyl which is optionally substituted by hydroxyl, (C₁-C₆)-alkoxy, cycloalkyl having from 3 to 8 carbon atoms or aryl having from 6 to 10 carbon atoms which, for its part, can be substituted, once to twice, identically or differently, by substituents which are selected from the

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group: group consisting of halogen, (C₁-C₆)-alkoxy, hydroxyl ~~or~~ and trifluoromethyl, or

denotes (C₁-C₈)-alkyl which is optionally substituted by a group of the formula -NR⁷R⁸,

in which

R⁷ and R⁸ are identical or different and denote hydrogen, (C₁-C₆)-alkyl or benzyl,

or

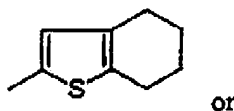
R⁴ denotes vinyl or allyl,

or

R⁴ denotes aryl having from 6 to 10 carbon atoms which is optionally substituted, once to twice, identically or differently, by substituents which are selected from the group consisting ~~of~~ of halogen, (C₁-C₆)-alkyl, (C₁-C₆)-alkoxy ~~or~~ and hydroxyl,

R⁵ denotes hydrogen or (C₁-C₄)-alkyl,

R⁶ denotes cycloalkyl having from 3 to 8 carbon atoms or a radical of the formula



aryl having from 6 to 10 carbon atoms or a 5- to 7-membered aromatic heterocycle having up to 3 heteroatoms selected from the series group

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consisting of S, N and/or O, it being possible for the ring systems which are listed here to be optionally substituted, once to several times, identically or differently, by substituents which are selected from the ~~group~~ group consisting of halogen, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, carboxyl, (C₁-C₆)-alkoxycarbonyl, (C₁-C₆)-alkyl and radicals of the formulae -SO₂-NR⁹R¹⁰ and -(CO)_a-NR¹¹R¹²,

in which

R⁹, R¹⁰, R¹¹ and R¹² are identical or different and denote hydrogen or (C₁-C₆)-alkyl,

and

a denotes a number 0 or 1,

or

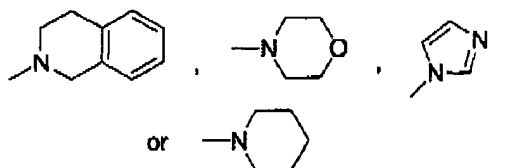
R⁶ denotes (C₁-C₈)-alkyl which is optionally substituted, once to twice, identically or differently, by substituents which are selected from the ~~group~~ group consisting of halogen, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, carboxyl, (C₁-C₆)-alkoxycarbonyl and aryl having from 6 to 10 carbon atoms, and a 5- to 7-membered aromatic heterocycles having up to 3 heteroatoms selected from the series group consisting of S, N and/or O, in which the ring systems can be optionally substituted, once to three times, identically or differently, by (C₁-C₆)-alkyl, halogen, (C₁-C₆)-alkoxy, (C₁-C₆)-alkoxycarbonyl, trifluoromethyl or by the radical -CO-NH₂,

or

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a¹
R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae



which, for their part, can be optionally substituted,

~~and the salts~~ or a pharmaceutically acceptable salt thereof,

with the exception, however, of the compound N-methyl-4-(4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)benzamide.

2. (currently amended) A The 6-carboxyphenyldihydropyridazinone derivative of claim 1,
wherein in the general formula (I) ~~as claimed in claim 1,~~

in which

A, D, E and G are identical or different and
represent hydrogen, fluorine, chlorine, bromine or trifluoromethyl,

R¹ and R² are identical or different and
represent hydrogen or represent methyl,

R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

in which

R⁴ denotes cyclopropyl, cyclopentyl or cyclohexyl or

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denotes (C₁-C₆)-alkyl which is optionally substituted by hydroxyl, (C₁-C₄)-alkoxy, cyclopropyl, cyclopentyl, cyclohexyl or phenyl which, for its part, can be substituted once to twice, identically or differently, by substituents selected from the ~~group~~: group consisting of fluorine, chlorine, bromine, (C₁-C₄)-alkoxy, hydroxyl or and trifluoromethyl, or

denotes (C₁-C₆)-alkyl which is optionally substituted by a group of the formula -NR⁷R⁸,

in which

R⁷ and R⁸ are identical or different and denote hydrogen or (C₁-C₄)-alkyl,

or

R⁴ denotes allyl,

R⁵ denotes hydrogen or (C₁-C₃)-alkyl,

R⁶ denotes cyclopropyl, cyclopentyl or cyclohexyl or
denotes phenyl, thienyl, thiazolyl, furyl or pyridyl, it being possible for the listed aromatic ring systems to be optionally substituted, once to twice, identically or differently, by substituents selected from the ~~group~~: group consisting of fluorine, chlorine, bromine, trifluoromethyl, hydroxyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, (C₁-C₄)-alkyl and radicals of the formulae -SO₂NR⁹R¹⁰ and -(CO)₂-NR¹¹R¹²,

in which

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R^9 , R^{10} , R^{11} and R^{12} are identical or different and denote hydrogen or (C₁-C₄)-alkyl,

and

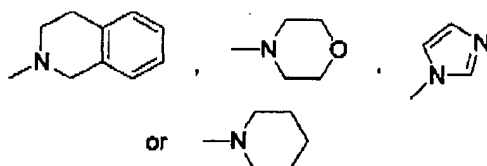
a denotes a number 0 or 1,

or

R^6 denotes (C₁-C₆)-alkyl which are optionally substituted once to twice, identically or differently, by substituents selected from the group: group consisting of fluorine, chlorine, bromine, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, (C₁-C₄)-alkoxycarbonyl, phenyl, pyridyl, naphthyl, furyl or and thiazolyl, it being possible for the ring systems to be optionally substituted, once to twice, identically or differently, by fluorine, chlorine, methyl, methoxycarbonyl, trifluoromethyl or by a radical of the formula -CO-NH₂,

or

R^5 and R^6 form, together with the nitrogen atom, cyclic radicals of the formulae



~~and the salts thereof,~~

~~with the exception, however, of the compound N-methyl 4-(4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)benzamide.~~

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contol . 3. (currently amended) ~~A~~ The 6-carboxyphenyldihydropyridazinone derivative of claim 1,
a¹ wherein in the general formula (I) as claimed in claim 1,

~~in which~~

A, D, E and G represent hydrogen,

R¹ and R² are identical or different and
represent hydrogen or represent methyl,

R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

in which

R⁴ denotes cyclopropyl, cyclopentyl or cyclohexyl or
denotes (C₁-C₅)-alkyl which is optionally substituted by (C₁-C₄)-alkoxy,
cyclopropyl, cyclopentyl, cyclohexyl or phenyl which, for its part, can be
substituted, once to twice, identically or differently, by substituents
selected from the ~~group:~~ group consisting of fluorine, chlorine, (C₁-C₄)-
alkoxy, hydroxyl ~~or~~ and trifluoromethyl, or

denotes (C₁-C₄)-alkyl which is optionally substituted by a group of the
formula -NR⁷R⁸,

in which

R⁷ and R⁸ are identical or different and denote hydrogen, benzyl or methyl,

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or

R^4 denotes allyl,

R^5 denotes hydrogen or (C₁-C₃)-alkyl,

R^6 denotes cyclopropyl, cyclopentyl or cyclohexyl or
denotes naphthyl, phenyl, thienyl, thiazolyl, furyl or pyridyl, the listed ring
systems being optionally substituted once to twice, identically or
differently, by substituents selected from the ~~group~~ group consisting of
fluorine, chlorine, bromine, trifluoromethyl, (C₁-C₃)-alkoxy, (C₁-C₃)-
alkoxycarbonyl, (C₁-C₃)-alkyl and radicals of the formulae -SO₂-NR⁹R¹⁰
and -(CO)_a-NR¹¹R¹²,

in which

R⁹, R¹⁰, R¹¹ and R¹² are identical or different and denote hydrogen or (C₁-C₄)-
alkyl,

and

a denotes a number 0 or 1,

or

R^6 denotes (C₁-C₆)-alkyl which is optionally substituted by substituents
selected from the ~~group~~ group consisting of fluorine, chlorine,
trifluoromethyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, phenyl, pyridyl,
naphthyl, furyl, thienyl ~~or~~ and thiazolyl, the ring systems optionally being

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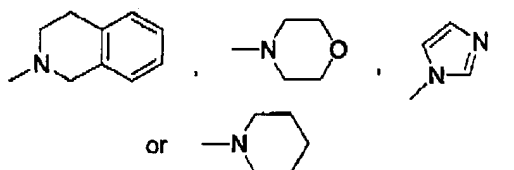
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substituted once to twice, identically or differently, by fluorine, chlorine, methyl, methoxycarbonyl or trifluoromethyl or by a radical of the formula -CO-NH₂,

or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae



and the salts thereof,

~~with the exception, however, of the compound N-methyl 4 (4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)benzamide.~~

4. (currently amended) A The 6-carboxyphenyldihydropyridazinone derivative of claim 1,
wherein in the general formula (I) as claimed in claim 1,

~~in which~~

A, D, E and G represent hydrogen,

R³ represents the radical -NR⁵R⁶, where R⁵ = H or methyl and R⁶ is as previously defined, defined in claim 1.

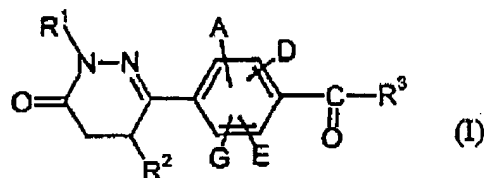
and the remaining radicals have the ~~previously mentioned meaning~~ meanings defined in claim 1.

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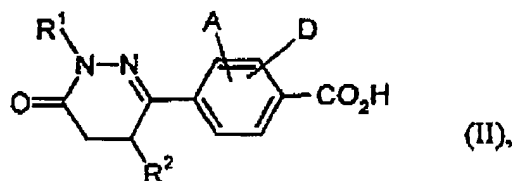
5. (currently amended) A process for preparing 6-carboxy-phenyl-dihydropyridazinone derivatives ~~as claimed in claims 1 to 4, of formula (I) as defined in claim 1~~



characterized in that

[A] in the case where R³ represents the radical of the formula -OR⁴ in ~~the above~~ general formula (I),

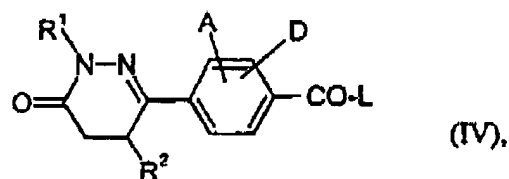
compounds of the general formula (II)



in which

A, D, R¹ and R² ~~have the abovementioned meaning, are as defined in claim 1,~~

are initially converted, by reaction with carboxylic acid-activating reagents, using customary methods, into the compounds of the general formula (IV)



in which

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a¹

A, D, R¹ and R² ~~have the above mentioned meaning,~~ are as defined in claim 1,

and

L represents an activating radical, ~~preferably chlorine or imidazolyl,~~

and, in a second step, reacted with compounds of the general formula (III)



in which

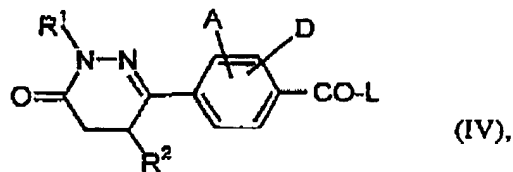
R⁴ ~~has the above mentioned meaning,~~ is as defined in claim 1,

in an inert solvents solvent, where appropriate in the presence of a base,

or

[B] in the case where R³ represents the radical of the formula -NR⁵R⁶ in the above general formula (I),

compounds of the general formula (II) are initially converted, by reaction with carboxylic acid-activating reagents, and using customary methods, into the compounds of the general formula (IV)



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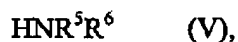
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a¹
in which

A, D, R¹ and R² ~~have the above mentioned meaning,~~ are as defined in claim 1.

and

L represents an activating radical, ~~preferably chlorine or imidazolyl,~~

and, in a second step, reacted with ~~amides~~ an amine of the general formula (V)



in which

R⁵ and R⁶ ~~have the above mentioned meaning,~~ are as defined in claim 1.

in an inert solvent solvents.

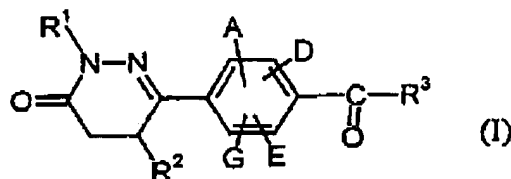
6. (currently amended) ~~A medicament or pharmaceutical composition which comprises at least one compound as claimed in claims 1 to 4 of claim 1, and also one or more pharmacologically harmless auxiliary and carrier substances acceptable excipients.~~

✓✓✓
7, 8, and 9 (cancelled)

a²
10. (currently amended) ~~The use of A method for prophylaxis or treatment of anemia comprising administering to a subject an effective amount of a 6-carboxyphenyldihydropyridazinone derivatives~~ derivative of the general formula (I)

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in which

A, D, E and G are identical or different and

represent hydrogen, halogen, trifluoromethyl or hydroxyl, or represent (C₁-C₆)-alkyl or represent (C₁-C₆)-alkoxy,

R¹ and R² are identical or different and

represent hydrogen or represent (C₁-C₆)-alkyl,

R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

in which

R⁴ denotes cycloalkyl having from 3 to 8 carbon atoms or (C₁-C₈)-alkyl which is optionally substituted by hydroxyl, (C₁-C₆)-alkoxy, cycloalkyl having from 3 to 8 carbon atoms or aryl having from 6 to 10 carbon atoms which, for its part, can be substituted, once to twice, identically or differently, by substituents which are selected from the ~~group~~ group consisting of halogen, (C₁-C₆)-alkoxy, hydroxyl ~~or~~ and trifluoromethyl, or

denotes (C₁-C₈)-alkyl which is optionally substituted by a group of the formula -NR⁷R⁸,

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in which

R^7 and R^8 are identical or different and denote hydrogen, (C_1-C_6) -alkyl or benzyl,

or

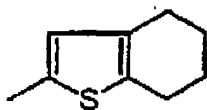
R^4 denotes vinyl or allyl,

or

R^4 denotes aryl having from 6 to 10 carbon atoms which is optionally substituted, once to twice, identically or differently, by substituents which are selected from the group consisting of: of halogen, (C_1-C_6) -alkyl, (C_1-C_6) -alkoxy or and hydroxyl,

R^5 denotes hydrogen or (C_1-C_4) -alkyl,

R^6 denotes cycloalkyl having from 3 to 8 carbon atoms or a radical of the formula



or

aryl having from 6 to 10 carbon atoms or a 5- to 7-membered aromatic heterocycle having up to 3 heteroatoms selected from the series group consisting of S, N and/or O, it being possible for the ring systems which are listed here to be optionally substituted, once to several times, identically or differently, by substituents which are selected from the group: group consisting of halogen, trifluoromethyl, hydroxyl, (C_1-C_6) -

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alkoxy, carboxyl, (C₁-C₆)-alkoxycarbonyl, (C₁-C₆)-alkyl and radicals of the formulae -SO₂-NR⁹R¹⁰ and -(CO)_a-NR¹¹R¹²,

in which

R⁹, R¹⁰, R¹¹ and R¹² are identical or different and denote hydrogen or (C₁-C₆)-alkyl,

and

a denotes a number 0 or 1,

or

R⁶ denotes (C₁-C₈)-alkyl which is optionally substituted, once to twice, identically or differently, by substituents which are selected from the ~~group~~ group consisting of halogen, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, carboxyl, (C₁-C₆)-alkoxycarbonyl, and aryl having from 6 to 10 carbon atoms, and a 5- to 7-membered aromatic ~~heterocycle~~ heterocycles having up to 3 heteroatoms selected from the series group consisting of S, N and ~~or~~ O, in which the ring systems can be optionally substituted, once to three times, identically or differently, by (C₁-C₆)-alkyl, halogen, (C₁-C₆)-alkoxy, (C₁-C₆)-alkoxycarbonyl, trifluoromethyl or by the radical -CO-NH₂,

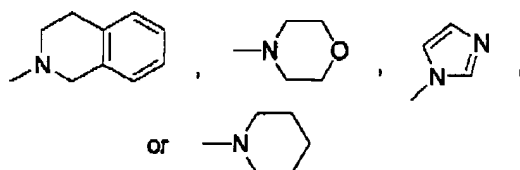
or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae

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a²



which, for their part, can be optionally substituted,

~~and the salts thereof, or a pharmaceutically acceptable salt thereof.~~

~~for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of anemias.~~

11. (currently amended) ~~The use of~~ The method of claim 10 wherein in the
6-carboxyphenyldihydropyridazinone ~~derivatives~~ derivative of the general formula (I) as
~~claimed in claim 10,~~
in which

A, D, E and G are identical or different and
represent hydrogen, fluorine, chlorine, bromine or trifluoromethyl,

R¹ and R² are identical or different and
represent hydrogen or represent methyl,

R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

in which

R⁴ denotes cyclopropyl, cyclopentyl or cyclohexyl or
denotes (C₁-C₆)-alkyl which is optionally substituted by hydroxyl, (C₁-C₄)-
alkoxy, cyclopropyl, cyclopentyl, cyclohexyl or phenyl which, for its part,

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can be substituted once to twice, identically or differently, by substituents selected from the ~~group~~: group consisting of fluorine, chlorine, bromine, (C₁-C₄)-alkoxy, hydroxyl ~~or~~ and trifluoromethyl, or

denotes (C₁-C₆)-alkyl which is optionally substituted by a group of the formula -NR⁷R⁸,

in which

R⁷ and R⁸ are identical or different and denote hydrogen or (C₁-C₄)-alkyl,

or

R⁴ denotes vinyl or allyl,

R⁵ denotes hydrogen or (C₁-C₃)-alkyl,

R⁶ denotes cyclopropyl, cyclopentyl or cyclohexyl or
denotes phenyl, thienyl, thiazolyl, furyl or pyridyl, it being possible for the listed aromatic ring systems to be optionally substituted, once to twice, identically or differently, by substituents selected from the ~~group~~: group consisting of fluorine, chlorine, bromine, trifluoromethyl, hydroxyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, (C₁-C₄)-alkyl and radicals of the formulae -SO₂NR⁹R¹⁰ and -(CO)_a-NR¹¹R¹²,

in which

R⁹, R¹⁰, R¹¹ and R¹² are identical or different and denote hydrogen or (C₁-C₄)-alkyl,

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and

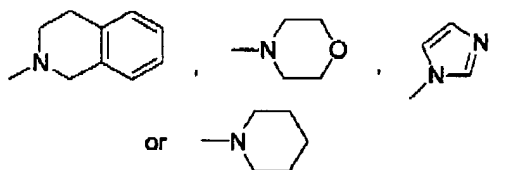
a denotes a number 0 or 1,

or

R⁶ denotes (C₁-C₆)-alkyl which are optionally substituted once to twice, identically or differently, by substituents selected from the ~~group~~ group consisting of fluorine, chlorine, bromine, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, (C₁-C₄)-alkoxycarbonyl, phenyl, pyridyl, naphthyl, furyl ~~or~~ and thiazolyl, it being possible for the ring systems to be optionally substituted, once to twice, identically or differently, by fluorine, chlorine, methyl, methoxycarbonyl, trifluoromethyl or by a radical of the formula -CO-NH₂,

or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae



which are in turn optionally ~~substituted~~, substituted.

~~and the salts thereof,~~

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~~for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of anemias.~~

12. (currently amended) ~~The use of~~ The method of claim 10 wherein in the
6-carboxyphenyldihydropyridazinone derivatives of the general formula (I) ~~as claimed in~~
~~claim 10;~~
~~in which~~

A, D, E and G represent hydrogen,

R¹ and R² are identical or different and
represent hydrogen or represent methyl,

R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

in which

R⁴ denotes cyclopropyl, cyclopentyl or cyclohexyl or
denotes (C₁-C₅)-alkyl which is optionally substituted by (C₁-C₄)-alkoxy,
cyclopropyl, cyclopentyl, cyclohexyl or phenyl which, for its part, can be
substituted, once to twice, identically or differently, by substituents
selected from the ~~group~~ group consisting of fluorine, chlorine, (C₁-C₄)-
alkoxy, hydroxyl ~~or~~ and trifluoromethyl, or

denotes (C₁-C₄)-alkyl which is optionally substituted by a group of the
formula -NR⁷R⁸,

in which

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R⁷ and R⁸ are identical or different and denote hydrogen, benzyl or methyl,

or

R⁴ denotes allyl,

R⁵ denotes hydrogen or (C₁-C₃)-alkyl,

R⁶ denotes cyclopropyl, cyclopentyl or cyclohexyl or
denotes naphthyl, phenyl, thienyl, thiazolyl, furyl or pyridyl, the listed ring
systems being optionally substituted once to twice, identically or
differently, by substituents selected from the ~~group:~~ group consisting of
fluorine, chlorine, bromine, trifluoromethyl, (C₁-C₃)-alkoxy, (C₁-C₃)-
alkoxycarbonyl, (C₁-C₃)-alkyl and radicals of the formulae -SO₂-NR⁹R¹⁰
and -(CO)_a-NR¹¹R¹²,

in which

R⁹, R¹⁰, R¹¹ and R¹² are identical or different and denote hydrogen or (C₁-C₄)-
alkyl,

and

a denotes a number 0 or 1,

or

R⁶ denotes (C₁-C₆)-alkyl which is optionally substituted by substituents
selected from the ~~group:~~ group consisting of fluorine, chlorine,

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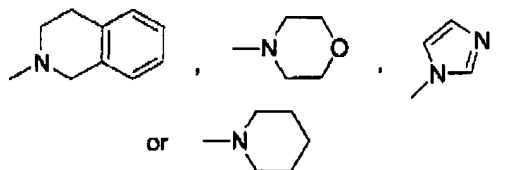
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trifluoromethyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, phenyl, pyridyl, naphthyl, furyl, thienyl or and thiazolyl, the ring systems optionally being substituted once to twice, identically or differently, by fluorine, chlorine, methyl, methoxycarbonyl or trifluoromethyl or by a radical of the formula -CO-NH₂,

or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae



which are in turn optionally ~~substituted~~, substituted.

~~and the salts thereof,~~

~~for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of anemias.~~

13. (currently amended) ~~The use of~~ The method of claim 10 wherein in the
6-carboxyphenyldihydropyridazinone derivatives of the general formula (I) ~~as claimed in~~
~~claim 10,~~
in which

A, D, E and G represent hydrogen,

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R³ represents the radical -NR⁵R⁶, where R⁵ = H or methyl and R⁶ is as ~~previously~~
~~defined,~~ defined in claim 10.

and the remaining radicals have the ~~previously given meaning,~~ are as defined in claim 10.

and the salts thereof,

~~for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or~~
~~treatment of anemias.~~

14. (currently amended) The ~~use~~ method as claimed in one of claims 10 to 13 ~~for preparing~~
~~medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of~~
wherein the anemia is selected from the group consisting of premature baby anemias,
anemias associated with chronic renal insufficiency, anemias following chemotherapy
and anemias in HIV patients.

15. (currently amended) The ~~use~~ method as claimed in one of claims 10 to 13 ~~for preparing~~
~~medicaments or pharmaceutical compositions for stimulating the~~ wherein the anemia is
erythropoiesis of individuals donating their own blood.

✓ ✓ ✓
16, 17, and 18 (canceled) ✓

a 3
19. (currently amended) The ~~use~~ method as claimed in one of claims ~~16 to 18~~ 10 to 15,
characterized in that the erythropoietin sensitizers are
6-carboxyphenyldihydropyridazinone derivative is administered orally.

a 4
20 (new) The process of claim 5 wherein in structure (IV), the activating radical L is chlorine or
imidazolyl.